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Re-evaluation Note

REV2017-25

Special Review of Diphenylamine and Its Associated End-use Products: Proposed Decision for Consultation

(publié aussi en français)

29 September 2017

This document is published by the Health Canada Pest Management Regulatory Agency. For further information, please contact:

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ISSN: 1925-0630 (print)
1925-0649 (online)

Catalogue number: H113-5/2017-25E (print version)
H113-5/2017-25E-PDF (PDF version)

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1.0 Introduction

Pursuant to subsection 17(2) of the *Pest Control Products Act*, the Pest Management Regulatory Agency (PMRA) has initiated a special review of pest control products containing diphenylamine based on the decision taken by the European Commission in 2012. The initiation of the special review under the *Pest Control Products Act* was announced in December 2013.¹

Pursuant to subsection 18(4) of the *Pest Control Products Act*, the PMRA has evaluated the aspect of concern that prompted the special review of pest control products containing diphenylamine. The aspect of concern was relevant to human health and pertained to dietary exposure.

2.0 Uses of Diphenylamine in Canada

Diphenylamine is registered for post-harvest treatment of apples in storage for reduction of scald, and applied by drenching, dipping, spraying or thermal fogging. Apples are treated within 15 days after harvesting. Certain product labels allow for a second treatment between the second and third months of storage. All currently registered products containing diphenylamine are considered in this special review (Appendix I).

3.0 Aspect of Concern that Prompted the Special Review

Based on the review of the 2012 European Commission decision,² the PMRA identified the aspect of concern that prompted the special review of diphenylamine as:

- Potential dietary risk.

4.0 PMRA Evaluation of the Aspect of Concern that Prompted the Special Review

Following the initiation of the special review of diphenylamine, the PMRA requested information related to the aspect of concern from provinces and other relevant federal departments and agencies in accordance with subsection 18(2) of the *Pest Control Products Act*. No information was received relevant to the aspect of concern. In addition, incident reports were searched for the active ingredient diphenylamine. As of 17 August 2017, there were no incident reports related to diphenylamine in the Canadian incident reporting database.

¹ Canada, 2013. Pest Management Regulatory Agency Re-evaluation Note REV2013-06, *Special Review Initiation of 23 Active Ingredients*.

² European Commission, 2012. Commission Implementing Regulation (EU) No 578/2012 of 29 June 2012 concerning the non approval of the active substance diphenylamine, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market.

Dietary exposure to diphenylamine may occur from consumption of treated fruit. To determine if exposure to diphenylamine in food is of concern the PMRA has conducted a quantitative dietary exposure assessment. In a dietary exposure assessment, the PMRA determines how much of a pesticide residue, including residues in meat and milk, may be ingested with the daily diet.

These dietary assessments are age-specific and incorporate the different eating habits of the population at various stages of life (infants, children, adolescents, adults and seniors). For example, the assessments take into account differences in children's eating patterns, such as food preferences, and the greater consumption of food relative to their body weight when compared to adults.

As all currently registered uses of diphenylamine are for the post-harvest phase, exposure through drinking water is not expected and drinking water was not included in the assessment. No appropriate endpoint attributable to a single dose for the general population (including children and infants) was identified; therefore an acute dietary risk assessment was not conducted. Further, diphenylamine is not expected to be carcinogenic; therefore a cancer dietary risk assessment was not required. Based on currently available information (USEPA 2015, USEPA 2006, USEPA 2005) target organs for diphenylamine are the liver, spleen and kidneys. There is no evidence of reproductive toxicity or increased susceptibility of fetuses or offspring compared to parental animals. The acceptable daily intake (ADI) for diphenylamine is 0.025 mg/kg bw/day based on a NOAEL of 2.5 mg/kg bw/day from a 2-year dog study and an uncertainty factor of 100-fold (10-fold for intra-species variation, 10-fold for inter-species extrapolation), which is considered protective of any potential adverse effects.

Chronic dietary exposure from food was estimated based on median level residues from apple post-harvest diphenylamine fumigation trials and MRL/tolerance level residues (Canada, 2013). The assessment includes both Canadian as well as US commodities, including pear and animal commodities.

The expected intake of residues was then compared to the ADI, which is the dose at which an individual could be exposed over the course of a lifetime and expect no adverse health effects. When the calculated intake of residues from all food sources (including water) is less than the ADI, then chronic dietary exposure is not of concern.

The chronic dietary exposure from all diphenylamine food uses for the representative population subgroups was below the ADI (less than 42.3% of the ADI), and therefore not of concern. The highest exposed population subgroup was all infants less than one year old.

As noted above, aggregate exposure from food and drinking water was not considered due to the timing of application of diphenylamine to apples (post-harvest).

Based on the above analysis, potential dietary exposure from the use of diphenylamine is not expected to be of concern under the current conditions of use. No additional risk mitigation measures are proposed.

5.0 Proposed Special Review Decision for Diphenylamine

Evaluation of available scientific information related to the aspect of concern indicated that the registered products containing diphenylamine do not pose potential risks of concern to human health. On this basis, the PMRA is proposing to confirm the current registration of products containing diphenylamine for sale and use in Canada pursuant to subsection 21(1) of the *Pest Control Products Act*.

This proposed special review decision is a consultation document.³ The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications (please see contact information on the cover page of this document).

6.0 Next Steps

Before making a special review decision on diphenylamine, the PMRA will consider all comments received from the public in response to this consultation document. A science-based approach will be applied in making a final decision on diphenylamine. The PMRA will then publish a special review decision document, which will include the decision, the reasons for it, a summary of the comments received on the proposed decision and the PMRA's response to these comments.

³ "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

**Appendix I Registered Products Containing Diphenylamine as of
17 August 2017**

Registration Number	Marketing Class	Registrant	Product Name
29505	Technical	Pace International LLC	DPA Super Refined Diphenylamine
29636	Technical	Decco U.S. Post-Harvest Inc.	Diphenylamine Technical
13471	Commercial	Decco U.S. Post-Harvest Inc.	No Scald DPA EC-283
18983	Commercial	Pace International, LLC	Shield DPA 15% Super Refined
30231	Commercial	Decco U.S. Post-Harvest Inc.	Decco No Scald DPA Aerosol
30410	Commercial	Pace International LLC	ecoFOG-100
31377	Commercial	Pace International LLC	ecoFOG-170 DPA

References

Published Information

PMRA Document Number	Reference
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2791832	United States, 2005. United States Environmental Protection Agency. PP# 0E6107: Human Health Risk Assessment for the Proposed Section 3 Use of Diphenylamine on Pear and for the Registration of a New Product and Method for the Application of Diphenylamine to Apples. 8/8/2005. EPA-HQ-OPP-2006-0731-0002.
2791834	United States, 2006. Federal Register / Vol. 71, No. 234 / Wednesday, December 6, 2006 / Proposed Rule. Environmental Protection Agency. Diphenylamine; Proposed Pesticide Tolerance. EPA-HQ-OPP-2006-0731-0001.
2791835	United States, 2015. United States Environmental Protection Agency. Diphenylamine Human Health Assessment Scoping Document in Support of Registration Review. December 10, 2015. EPA-HQ-OPP-2015-0749-0006.